Timing of Rotavirus Vaccine Doses and Incidence of Severe Rotavirus Gastroenteritis among Vaccinated Infants in Low- and Middle-Income Countries

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Supplemental File

Additional Information on Methods

Infants contributed person-time to each schedule for each aspect of timing from 12 weeks of age until the earliest of any of the following instances occurred: 1) the infant was lost to follow-up, 2) the infant experienced a severe RVGE event, or 3) the timing of the infant's actual doses deviated from the predefined timing requirements allowed for that specific schedule. eTable 1 includes detailed information on inclusion and censoring from each schedule, and eTable 2 illustrates detailed examples of two hypothetical infants in each trial and the persontime contributed for each schedule for each aspect of timing.

eTable 1. Detailed description entry, follow-up and censoring for predefined schedules for each aspect of timing.

Aspect of	RV	Age at	Timing of	Timing of	5	• *
Timing	Туре	Dose 1	Dose 2	Dose 3	Description of Entry, Follow-up, and Censor	
					Infants with 1st dose at 3, 4, 5, or 6 wks of a and continue follow-up until severe RVGE, censoring. Infants are censored at the earlie of the following:	end of study, or
First dose with		3 – 6	4 – 6 wks	4 – 6 wks	Reason for Censoring	Time of Censoring
4 – 6 weeks	RV5	wks of	after 1st	after 2 nd	Lost to follow-up/dropout	Time of dropout
between doses	RVS	age	dose	dose	Receipt of 2 nd dose < 4 wks after 1 st dose	Time of 2 nd dose
out well doses			4050	4050	No 2 nd dose by 6 wks after 1 st dose	6 wks after 1st dose
					Receipt of 3 rd dose < 4 wks after 2 nd dose	Time of 3 rd dose
					No 3 rd dose by 6 wks after 1 st dose	6 wks after 2 nd dose
					Infants with 1st dose at 7, 8, or 9 wks of age and continue follow-up until severe RVGE, censoring. Infants are censored at the earlie of the following:	end of study, or st occurrence of any
First dose with		7 – 9	4-6 wks	4-6 wks	Reason for Censoring	Time of Censoring
4-6 weeks	RV5	wks of	after 1st	after 2 nd	Lost to follow-up/dropout	Time of dropout
between doses		age	dose	dose	Receipt of 2^{nd} dose < 4 wks after 1^{st} dose	Time of 2 nd dose
					No 2 nd dose by 6 wks after 1 st dose	6 wks after 1 st dose
					Receipt of 3 rd dose < 4 wks after 2 nd dose	Time of 3 rd dose
					No 3 rd dose by 6 wks after 1 st dose	6 wks after 2 nd dose
					Infants with 1st dose at 10, 11, or 12 wks of group and continue follow-up until severe F or censoring. Infants are censored at the ear any of the following:	RVGE, end of study, liest occurrence of
First dose with		10 - 12	4-6 wks	4-6 wks	Reason for Censoring	Time of Censoring
4-6 weeks	RV5	wks of	after 1st	after 2 nd	Lost to follow-up/dropout	Time of dropout
between doses		age	dose	dose	Receipt of 2 nd dose < 4 wks after 1 st dose	Time of 2 nd dose
					No 2 nd dose by 6 wks after 1 st dose	6 wks after 1 st dose
					Receipt of 3 rd dose < 4 wks after 2 nd dose	Time of 3 rd dose
					No 3 rd dose by 6 wks after 1 st dose	6 wks after 2 nd dose
					Infants with 1st dose at 10, 11, or 12 wks of group and continue follow-up until severe F or censoring. Infants are censored at the ear any of the following:	RVGE, end of study, liest occurrence of
First dose with			4-6 wks		Reason for Censoring	Time of Censoring
4-6 weeks	RV1	wks of	after 1st	NA	Lost to follow-up/dropout	Time of dropout
between doses		age	dose		Receipt of 2 nd dose < 4 wks after 1 st dose	Time of 2 nd dose
					No 2 nd dose by 6 wks after 1 st dose	6 wks after 1 st dose
		12			Infants missing first RV1 or with 1st dose > in this group and continue follow-up until s study, or censoring. Infants are censored at occurrence of any of the following: Reason for Censoring	evere RVGE, end of the earliest
First dose with	D. T. T.	13 – 16	4-6 wks	27.4		Time of Censoring
4 – 6 weeks	RV1	wks of	after 1st	NA	Lost to follow-up/dropout	Time of dropout
between doses		age	dose		No 1st dose by 16 wks of age	16 wks of age
					Receipt of 2 nd dose < 4 wks after 1 st dose	Time of 2 nd dose
					No 2 nd dose by 6 wks after 1 st dose	6 wks after 1 st dose

Aspect of Timing	RV Type	Age at Dose 1	Timing of Dose 2	Timing of Dose 3	Description of Entry, Follow-up, and Cens	soring*
Tilling	1 ypc	DUSC 1	DUSC 2	Dose 3	Infants with 1 st dose at < 6 wks of age beg continue follow-up until severe RVGE, en censoring. Infants are censored at the earli of the following:	d of study, or
					Reason for Censoring	Time of Censoring
					Lost to follow-up/dropout	Time of dropout
First dose	RV5	< 6 wks of age	≤ 10 wks after 1st	$\leq 10 \text{ wks}$ after 2^{nd}	No 2 nd dose by 10 wks after 1 st dose	10 wks after 1 st dose
		or age	dose	dose	No 3 rd dose by 10 wks after 2 nd dose	10 wks after 2 nd dose
					Infanta with 18 Jacout > 6 who of one has	
					Infants with 1 st dose at ≥ 6 wks of age beg continue follow-up until severe RVGE, en censoring. Infants are censored at the earlier of the following section of the following section.	d of study, or
					of the following:	TimesCC
					Reason for Censoring	Time of Censoring
			≤ 10 wks	≤ 10 wks	Lost to follow-up/dropout	Time of dropout 10 wks after 1st
First dose	RV5	\geq 6 wks of age	after 1st	after 2 nd	No 2 nd dose by 10 wks after 1 st dose	dose
		or uge	dose	dose	No 3 rd dose by 10 wks after 2 nd dose	10 wks after 2 nd dose
					Infants with 1 st dose at < 10 wks of age be continue follow-up until severe RVGE, en censoring. Infants are censored at the earli	d of study, or
					of the following: Reason for Censoring	Time of Censoring
		. 10	< 10 1	< 10 1	Lost to follow-up/dropout	Time of dropout
First dose	RV5	< 10 wks of	$\leq 10 \text{ wks}$ after 1^{st}	$\leq 10 \text{ wks}$ after 2^{nd}	No 2 nd dose by 10 wks after 1 st dose	10 wks after 1 st dose
		age	dose	dose	No 3 rd dose by 10 wks after 2 nd dose	10 wks after 2 nd dose
					Infants with 1 st dose at ≥ 10 wks of age be continue follow-up until severe RVGE, en censoring. Infants are censored at the earli of the following:	d of study, or lest occurrence of any
					Reason for Censoring	Time of Censoring
					Lost to follow-up/dropout	Time of dropout
First dose	RV5	≥ 10 wks of	≤ 10 wks after 1 st	$\leq 10 \text{ wks}$ after 2^{nd}	No 2 nd dose by 10 wks after 1 st dose	10 wks after 1 st dose
	K V J	age	dose	dose	No 3 rd dose by 10 wks after 2 nd dose	10 wks after 2 nd
						dose

Aspect of Timing	RV Type	Age at Dose 1	Timing of Dose 2	Timing of Dose 3	Description of Entry, Follow-up, and Cens	oring*
Timing	турс	Dose 1	Dose 2	Dose 3	Infants with 1 st dose at ≤ 7 wks of age begi continue follow-up until severe RVGE, encensoring. Infants are censored at the earlie of the following:	d of study, or
					Reason for Censoring	Time of Censoring
					Lost to follow-up/dropout	Time of dropout
		< 7 mlso			No 2 nd dose by 11 wks of age	11 wks of age
Last dose	RV5	\leq 7 wks of age	≤ 11	≤ 15	No 3 rd dose by 15 wks of age	15 wks of age
or age						
					All infants begin in this group and continue severe RVGE, end of study, or censoring.	Infants are censored at
					the earliest occurrence of any of the follow	
					Reason for Censoring	Time of Censoring
					Lost to follow-up/dropout	Time of dropout
		≤ 12	≤ 10 wks	> 15 &	No 2 nd dose by 10 wks after 1 st dose	10 wks after 1st dose
Last dose	RV5	wks of	after 1st	$\leq 10 \text{ wks}$	Receipt of 3^{rd} dose ≤ 15 wks of age	Time of 3 rd dose
		age	dose	after 2 nd dose	No 3 rd dose by 10 wks after 2 nd dose	10 wks after 2 nd
				dose	1 To 5 dose by 10 wks after 2 dose	dose
					Infants with 1 st dose at ≤ 11 wks of age beg continue follow-up until severe RVGE, encensoring. Infants are censored at the earlier of the following:	d of study, or est occurrence of any
					Reason for Censoring Lost to follow-up/dropout	Time of Censoring Time of dropout
		≤11			No 2 nd dose by 15 wks of age	15 wks of age
Last dose	RV1	wks of age	≤ 15 wks of age	NA		
					All infants begin in this group and continu- severe RVGE, end of study, or censoring. In the earliest occurrence of any of the follow	Infants are censored at
					Reason for Censoring	Time of Censoring
			\ 151		Lost to follow-up/dropout	Time of dropout
		≤ 16	> 15 wks of age &		No 1 st dose by 16 wks of age	16 wks of age
Last dose	RV1	≥ 10 wks of	< 10 wks	NA	Receipt of 2 nd dose \le 15 wks of age	Time of 2 nd dose 10 wks after 1 st
		age	after 2 nd		No 2 nd dose by 10 wks after 1 st dose	dose
			dose			dosc

Aspect of Timing	RV Type	Age at Dose 1	Timing of Dose 2	Timing of Dose 3	Description of Entry, Follow-up, and Censor	oring*
	-7F-				All infants begin in this group and continue for RVGE, end of study, or censoring. Infants are earliest occurrence of any of the following:	censored at the
Intomial		≤ 12	4 wks	4 wks	Reason for Censoring	Time of Censoring
Interval	RV5	wks of	after 1st	after 2 nd	Lost to follow-up/dropout	Time of dropout
between doses		age	dose	dose	Receipt of 2 nd dose < 4 wks after 1 st dose	Time of 2 nd dose
					No 2 nd dose by 4 wks after 1 st dose	4 wks after 1st dose
					Receipt of 3 rd dose < 4 wks after 2 nd dose	Time of 3 rd dose
					No 3 rd dose by 4 wks after 2 nd dose	4 wks after 2 nd dose
		≤ 12	4 wks	5 wks	All infants begin in this group and continue fo	
Interval between doses	RV5	wks of	after 1st	after 2 nd	RVGE, end of study, or censoring. Infants are earliest occurrence of any of the following:	
		age			Reason for Censoring	Time of Censoring
Interval		≤ 12	5 wks	4 wks	Lost to follow-up/dropout	Time of dropout
between doses	RV5	wks of	after 1st	after 2 nd	Receipt of 2 nd dose < 4 wks after 1 st dose	Time of 2 nd dose
between doses		age	dose	dose	No 2 nd dose by 5 wks after 1 st dose	5 wks after 1 st dose
					Receipt of 3^{rd} dose < 4 wks after 2^{rd} dose	Time of 3 rd dose
Interval		≤ 12	5 wks	5 wks	Receipt of 3 rd dose < 4 wks after 2 dose Receipt of 3 rd dose at 4 wks after 2 nd dose	Time of 3 rd dose
between doses	RV5	wks of	after 1st	after 2 nd	when 2 nd dose received 4 wks after 1 st dose	Time of 5 dose
between doses		age	dose	dose		7 1 C 2nd 1
					No 3 rd dose at by 5 wks after 2 nd dose	5 wks after 2 nd dose
Intomial		≤ 12	4 wks	6 wks	All infants begin in this group and continue for	
Interval	RV5	wks of	after 1st	after 2 nd	RVGE, end of study, or censoring. Infants are	censored at the
between doses		age	dose	dose	earliest occurrence of any of the following:	
			+		Reason for Censoring	Time of Censoring
Interval	D1/5	≤12	5 wks	6 wks	Lost to follow-up/dropout	Time of dropout
between doses	RV5	wks of	after 1st	after 2 nd	Receipt of 2 nd dose < 4 wks after 1 st dose	Time of 2 nd dose
		age	dose	dose	No 2 nd dose by 6 wks after 1 st dose	6 wks after 1st dose
		≤ 12	6 wks	4 wks	Receipt of 3 rd dose < 4 wks after 2 nd dose	Time of 3 rd dose
Interval	RV5	wks of	after 1st	after 2 nd	Receipt of 3 rd dose at 4 wks after 2 nd dose	Time of 3 rd dose
between doses	10,0	age	dose	dose	when 2 nd dose received 4 or 5 wks after 1 st	Time of a dose
					dose	
Interval		≤ 12	6 wks	5 wks	Receipt of 3 rd dose at 5 wks after 2 nd dose	Time of 3 rd dose
between doses	RV5	wks of	after 1st	after 2 nd	when 2 nd dose received 4 or 5 wks after 1 st	Time of 5 dose
between doses		age	dose	dose	dose	
		≤ 12	6 wks	6 wks	No 3 rd dose by 6 wks after 2 nd dose	6 wks after 2 nd dose
Interval	RV5	wks of	after 1st	after 2 nd	140 5 dose by 6 was after 2 dose	o was unter 2 dose
between doses	10,0	age	dose	dose		
		uge	dose	dose	A 11 in factor 1, a significant in this according to the second of the s	11
					All infants begin in this group and continue for RVGE, end of study, or censoring. Infants are	
					earliest occurrence of any of the following:	censored at the
T., 4.,		≤ 16	4 wks		Reason for Censoring	Time of Censoring
Interval	RV1	wks of	after 1st	NA		
between doses		age	dose		Lost to follow-up/dropout	Time of dropout
					No 1st dose by 16 wks of age	16 wks of age
					Receipt of 2 nd dose < 4 wks after 1 st dose	Time of 2 nd dose
					No 2 nd dose by 4 wks after 1 st dose	4 wks after 1st dose
					All infants begin in this group and continue for	
					RVGE, end of study, or censoring. Infants are	censored at the
		< 16	5 wks		earliest occurrence of any of the following:	
Interval	RV1	≤ 16 wks of	after 1st	NA	Reason for Censoring	Time of Censoring
between doses	IX V I			INA	Lost to follow-up/dropout	Time of dropout
		age	dose		No 1st dose by 16 wks of age	16 wks of age
					Receipt of 2 nd dose < 5 wks after 1 st dose	Time of 2 nd dose
					No 2 nd dose by 5 wks after 1 st dose	5 wks after 1st dose
					All infants begin in this group and continue for	
					RVGE, end of study, or censoring. Infants are	
					earliest occurrence of any of the following:	constitut at the
Interval		≤ 16	6 wks		Reason for Censoring	Time of Censoring
Interval	RV1	wks of	after 1st	NA		
between doses		age	dose		Lost to follow-up/dropout	Time of dropout
					No 1st dose by 16 wks of age	16 wks of age
					Receipt of 2 nd dose < 6 wks after 1 st dose	Time of 2 nd dose
	Ī				No 2 nd dose by 6 wks after 1 st dose	6 wks after 1st dose

Aspect of Timing	RV Type	Age at Dose 1	Timing of Dose 2	Timing of Dose 3	Description of Entry, Follow-up, and Censor	-
Number of doses ≥ 10 weeks of age	RV5	< 10 wks of age	< 10 wks of age	< 10 wks of age	All Infants with 1st dose at < 10 wks of age be continue follow-up until severe RVGE, end of Infants are censored at the earliest occurrence following: Reason for Censoring	f study, or censoring.
					Lost to follow-up/dropout	Time of dropout
					Receipt of 2^{nd} dose ≥ 10 wks of age	Time of 2 nd dose
Number of doses ≥ 10 weeks of age	RV5	< 10 wks of age	< 10 wks of age	No 3 rd dose	Receipt of 3^{rd} dose ≥ 10 wks of age	Time of 3 rd dose
Number of doses ≥ 10 weeks of age	RV5	< 10 wks of age	No 2 nd dose	No 3 rd dose		
Number of		≥ 10	No 2 nd	No 3 rd	All Infants begin in this group and continue for RVGE, end of study, or censoring. Infants are earliest occurrence of any of the following:	ollow-up until severe censored at the
$doses \ge 10$	RV5	wks of	dose	dose	Reason for Censoring	Time of Censoring
weeks of age		age	dose	dose	Lost to follow-up/dropout	Time of dropout
					Receipt of 3 rd dose < 10 wks of age	Time of 3rd dose
					Receipt of 2 nd dose when 1 st dose received	Time of 2 nd dose
Number of doses ≥ 10 weeks of age	RV5	< 10 wks of	≥ 10 & ≤ 32	No 3 rd dose	≥ 10 wks of age Receipt of 3 rd dose when 2 nd dose received ≥ 10 wks of age	Time of 3 rd dose
weeks of age		age			No 2 nd dose by 32 wks of age when 1 st dose received < 10 wks of age	32 wks of age
				≥ 10 wks	No 3 rd dose by 32 wks of age when 2 nd dose received < 10 wks of age	32 wks of age
Number of doses ≥ 10 weeks of age	RV5	< 10 wks of age	< 10 wks of age	of age & ≤ 32 wks of age		
Number of		≥ 10	≥ 10 wks of age &	No 3 rd	All Infants begin in this group and continue for RVGE, end of study, or censoring. Infants are earliest occurrence of any of the following:	
doses ≥ 10	RV5	wks of	\leq 32 wks	dose	Reason for Censoring	Time of Censoring
weeks of age	1	age	of age		Lost to follow-up/dropout	Time of dropout
	1				Receipt of 2 nd dose < 10 wks of age	Time of 2 nd dose
Number of		< 10	≥ 10 wks of age &	≥ 10 wks of age &	No 2^{nd} dose by 32 wks of age Receipt of 3^{rd} dose when 1^{st} dose and 2^{nd} dose received ≥ 10 wks of age	32 wks of age Time of 3 rd dose
doses ≥ 10 weeks of age	RV5	wks of age	≤ 32 wks of age	≤ 32 wks of age	No 3 rd dose by 32 wks of age when 1 st dose received < 10 wks of age and 2 nd dose received ≥ 10 wks of age	32 wks of age
Number of doses ≥ 10	RV5	≥ 10 wks of	≥ 10 wks of age &	≥ 10 wks of age &	All Infants with 1 st dose at \geq 10 wks of age be continue follow-up until severe RVGE, end of Infants are censored at the earliest occurrence following:	f study, or censoring. of any of the
weeks of age		age	\leq 32 wks	\leq 32 wks	Reason for Censoring	Time of Censoring
Julia of ago	1		of age	of age	Lost to follow-up/dropout	Time of dropout
	1				No 2 nd dose by 32 wks of age	32 wks of age
			/5 mantavala		No 3 rd dose by 32 wks of age	32 wks of age

RV1, monovalent rotavirus vaccine; RV5, pentavalent rotavirus vaccine; Wks, weeks; NA, not applicable *Censoring for those not receiving a first dose of vaccine is not described for the RV5 trial; all infants in the RV5 trial received at least 1 dose of vaccine, but some infants in the RV1 trial did not receive a dose of vaccine.

eTable 2. Example of entry, follow-up, and censoring for predefined schedules for each aspect of timing for two hypothetical infants receiving RV5 (infants A and B) and RV1 (infants C and D). Follow-up is indicated by gray.

Aspect of		RV	Age a	t Dose (v	veeks)		Age	in we	eks						
Timing	Infant	Type	Dose 1	Dose 2	Dose 3	Predefined Schedules	12	13	14	15	16	17	18	19	20
	A	RV5	5	10	18	3-6 weeks with 4-6 week intervals 7-9 weeks with 4-6 week intervals 10-12 weeks with 4-6 week intervals									
First dose with 4 – 6 weeks	В	RV5	10	16	20	3-6 weeks with 4-6 week intervals 7-9 weeks with 4-6 week intervals 10-12 weeks with 4-6 week intervals									->
between doses	С	RV1	10	15		10-12 weeks with 4-6 week intervals 13-16 weeks with 4-6 week intervals									->
	D	RV1	14	18		10-12 weeks with 4-6 week intervals 13-16 weeks with 4-6 week intervals									->
First dose	A	RV5	5	10	18	1^{st} dose < 6 weeks 1^{st} dose \geq 6 weeks									->
	В	RV5	10	16	20	1^{st} dose < 6 weeks 1^{st} dose ≥ 6 weeks									->
	A	RV5	5	10	18	3^{rd} dose ≤ 15 weeks 3^{rd} dose ≥ 15 weeks									->
Last dose	В	RV5	10	10 16	20	3^{rd} dose ≤ 15 weeks 3^{rd} dose ≥ 15 weeks 2^{nd} dose ≤ 15 weeks									-> ->
	С	RV1	10	15		$2^{\text{nd}} \text{ dose} \le 15 \text{ weeks}$ $2^{\text{nd}} \text{ dose} > 15 \text{ weeks}$ $2^{\text{nd}} \text{ dose} \le 15 \text{ weeks}$									->
	D	RV1	14	18		$\frac{2^{\text{nd}} \text{ dose} \leq 15 \text{ weeks}}{2^{\text{nd}} \text{ dose} > 15 \text{ weeks}}$ Both 4 weeks									->
	A	RV5	5	10	18	≥ 1 of 5 weeks ≥ 1 of 6 weeks									
Interval between	В	RV5	10	16	20	Both 4 weeks ≥ 1 of 5 weeks ≥ 1 of 6 weeks									->
doses	С	RV1	10	15		4 weeks 5 weeks 6 weeks									->
	D	RV1	14	18		4 weeks 5 weeks 6 weeks									->
Number of doses ≥ 10	A	RV5	5	10	18	1 dose at \geq 10 weeks 2 doses at \geq 10 weeks 3 doses at \geq 10 weeks									->
weeks of age	В	RV5	10	16	20	1 dose at \geq 10 weeks 2 doses at \geq 10 weeks 3 doses at \geq 10 weeks									->

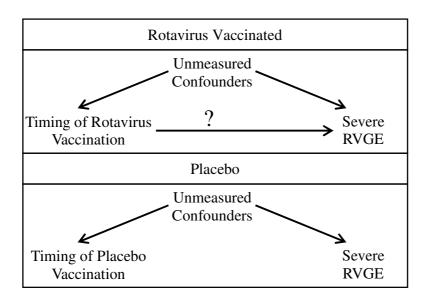
eTable 3. Number of expected severe RVGE episodes that would occur if altering vaccination schedules had no benefit.

nua no ochem.							
	Expected Increase in RVGE Episodes						
Cohort	per 1,000 Infants (95% CI)*						
Conort	RV1	RV5					
	6/10 vs. 10/14	6/10/14 vs. 8/12/16					
Cohort 1 [†]	5 (1, 8)	2 (0, 4)					
Cohort 2 [‡]	1 (0, 2)	0 (0, 1)					

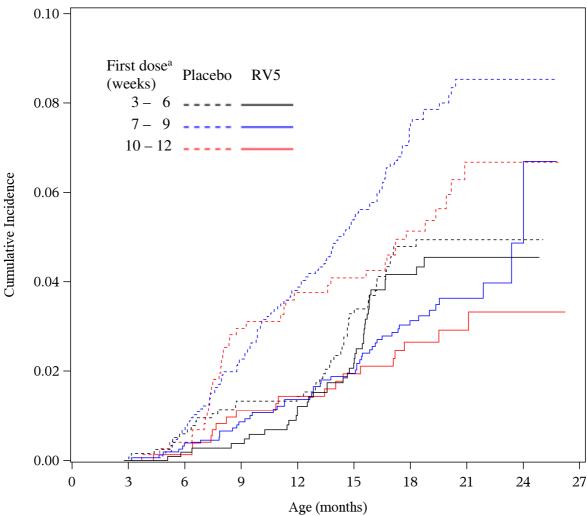
^{*}Estimates assume infants are fully protected at two weeks following the final dose of vaccine. Therefore, the expected increase is for the period from 12 to 16 weeks (RV1) and 16 to 18 weeks (RV5). These estimates also assume the severe RVGE episodes would be prevented had infants been vaccinated at 6/10 (RV1) or 6/10/14 (RV5) weeks and that there is no partial protection for an incomplete series for later vaccine schedules.

[†] Estimates for shifting RV1 or RV5 schedules using the placebo arm in RV1 Trial.

[‡] Estimates for shifting RV1 or RV5 schedules using the placebo arm in RV5 Trial.



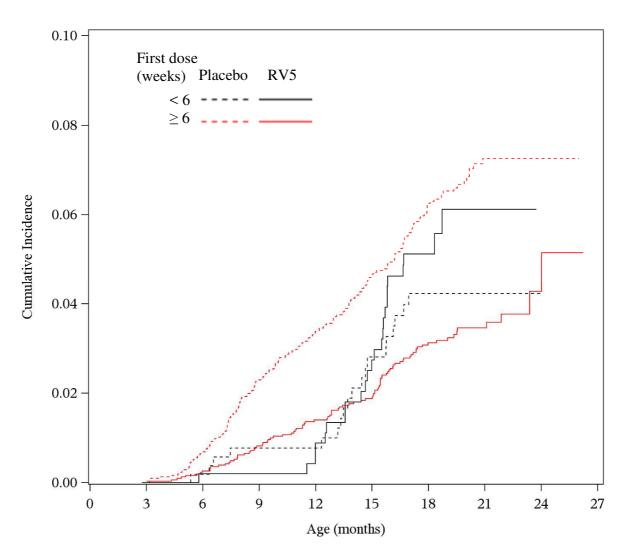
eFigure 1. Two directed acyclic graphs in the rotavirus vaccinated (top panel) and placebo (bottom panel) arms. We are interested in the effect of timing of rotavirus vaccination on incidence of severe RVGE. However, unmeasured confounders affecting both the timing of rotavirus vaccination and incidence of severe RVGE may make it appear that there is an association when one does not exist. In the placebo arm, the timing of placebo doses should not influence the incidence of severe RVGE. However, if there is an association between timing of placebo vaccination and severe RVGE, this would be due to unmeasured confounders. If we assume the same unmeasured confounders exist in both treatment arms (treatments were blinded), then we can adjust for unmeasured confounders in the rotavirus vaccinated arm by calibrating the estimates from the rotavirus vaccinated arm with the estimates from the placebo arm. This calibration would result in the removal of any effect due to confounders.



^a with 4-6 weeks between doses

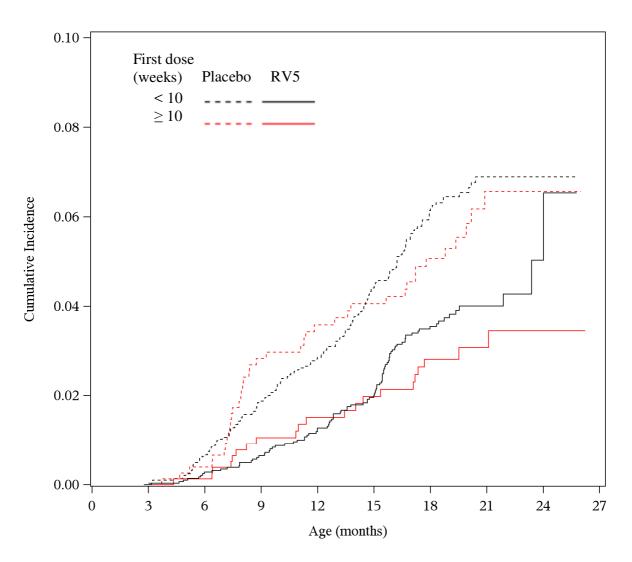
Vaccine Type	Age of first dose (weeks) with 4-6 weeks between doses				N	
	3 – 6	1,167	1,073	943	640	7
RV5	7 – 9	1,669	1,516	1,351	1,003	52
	10 - 12	784	720	600	527	45
	3 - 6	1,250	1,134	980	687	9
Placebo	7 – 9	1,589	1,451	1,293	948	64
	10 - 12	780	713	590	514	39

eFigure 2. Cumulative incidence of severe rotavirus gastroenteritis by age of first dose (weeks) with 4-6 week intervals between subsequent doses in the placebo and RV5 vaccinated arms. Number at risk at 12 weeks, 6 months, 12 months, 18 months, and 24 months of age for schedule is below the x-axis.



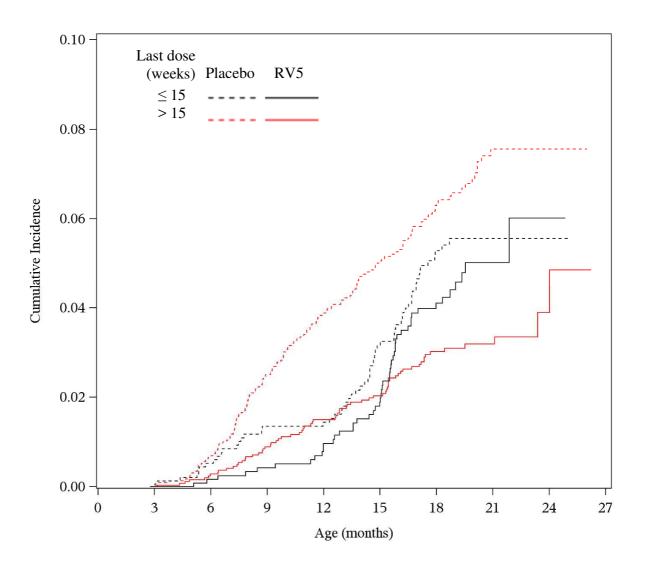
Vaccine Type	Age of first dose (weeks)				N	
RV5	< 6	519	506	432	255	0
KVJ	≥ 6	3,147	3,063	2,700	2,055	109
Placebo	< 6	548	534	445	274	0
	≥6	3,127	3,011	2,640	1,993	114

eFigure 3. Cumulative incidence of severe rotavirus gastroenteritis by age of first dose (< 6 weeks vs. \ge 6 weeks) in the placebo and RV5 vaccinated arms. Number at risk at 12 weeks, 6 months, 12 months, 18 months, and 24 months of age for each arm is below the x-axis.



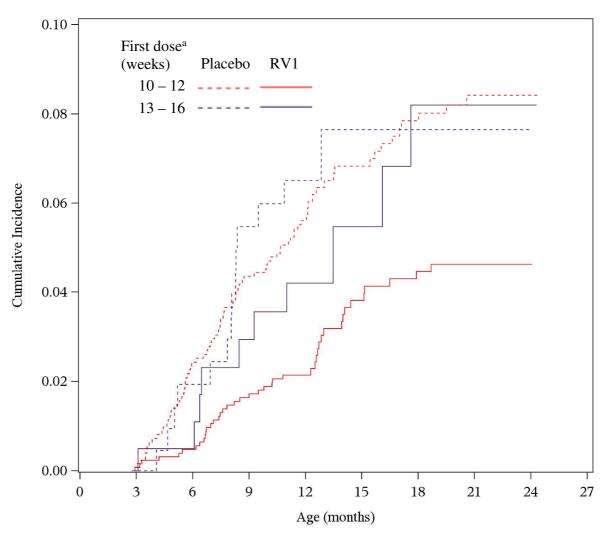
Vaccine Type	Age of first dose (weeks)				N	
DV5	< 10	2,882	2,805	2,492	1,754	63
RV5	≥ 10	784	764	640	556	46
Dlagabo	< 10	2,895	2,798	2,465	1,733	74
Placebo	≥ 10	780	747	620	534	40

eFigure 4. Cumulative incidence of severe rotavirus gastroenteritis by age of first dose (< 10 weeks vs. \geq 10 weeks) in the placebo and RV5 vaccinated arms. Number at risk at 12 weeks, 6 months, 12 months, 18 months, and 24 months of age for each arm is below the x-axis.



Vaccine Type	Age of last dose (weeks)		N							
RV5	≤ 15	1,527	1,216	1,087	778	9				
KVJ	> 15	3,520	2,353	2,045	1,532	100				
Dlagaba	≤ 15	1,596	1,253	1,104	803	12				
Placebo	> 15	3,534	2,292	1,981	1,464	102				

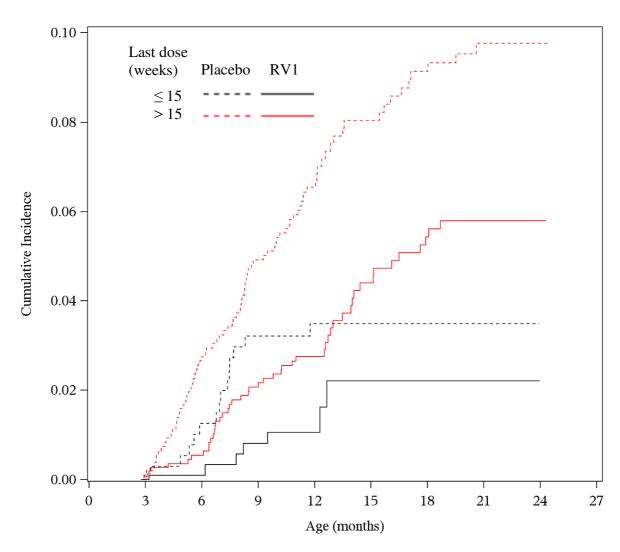
eFigure 5. Cumulative incidence of severe rotavirus gastroenteritis by age of last dose (\leq 15 weeks vs. > 15 weeks) in the placebo and RV5 vaccinated arms. Number at risk at 12 weeks, 6 months, 12 months, 18 months, and 24 months of age for each arm is below the x-axis.



^a with 4-6 weeks between doses

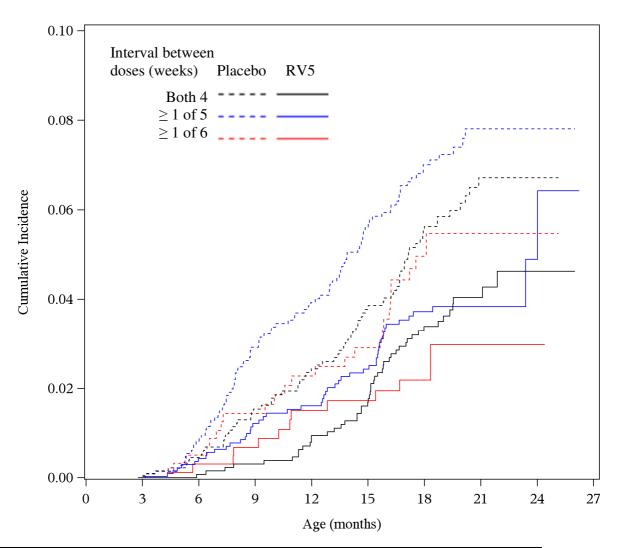
Vaccine Type	Age of first dose (weeks) with 4-6 weeks between doses				N	
RV1	10 - 12	1,299	1,212	767	573	7
KVI	13 – 16	207	166	100	67	1
Dlaasha	10 - 12	1,255	1,128	708	530	6
Placebo	13 – 16	253	196	107	73	1

eFigure 6. Cumulative incidence of severe rotavirus gastroenteritis by age of first dose with a 4-6 weeks between doses in the placebo and RV1 vaccinated arms. Number at risk at 12 weeks, 6 months, 12 months, 18 months, and 24 months of age for schedule is below the x-axis.



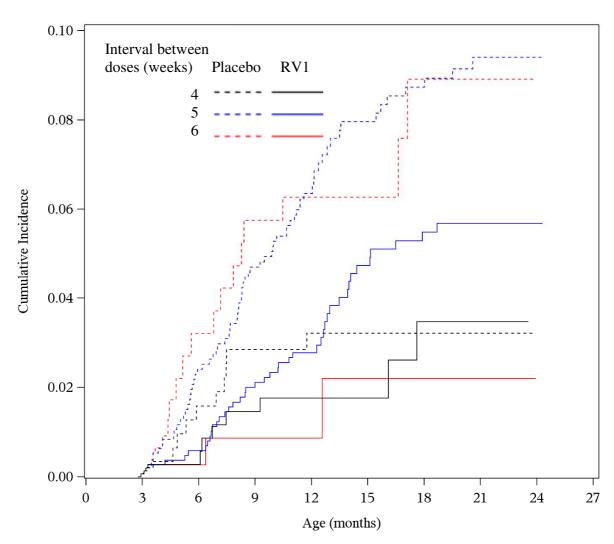
Vaccine Type	Age of last dose (weeks)	N				
RV5	≤ 15	1,048	420	218	149	0
	> 15	1,559	1,056	702	531	8
Placebo	≤ 15	998	408	220	152	0
	> 15	1,553	996	636	481	7

eFigure 7. Cumulative incidence of severe rotavirus gastroenteritis by age of last dose (\leq 15 weeks vs. > 15 weeks) in the placebo and RV1 vaccinated arms. Number at risk at 12 weeks, 6 months, 12 months, 18 months, and 24 months of age for each arm is below the x-axis.



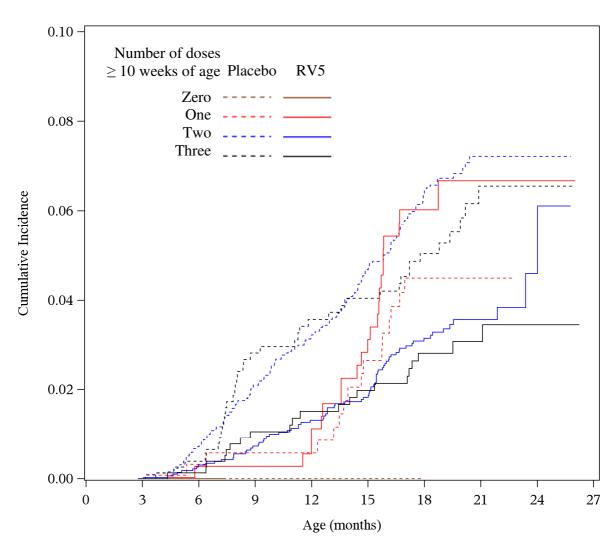
	Intervals							
Vaccine	between	N						
Type	doses							
	(weeks)							
RV5	Both 4	2,589	1,310	1,219	1,003	39		
	$\geq 1 \text{ of } 5$	3,345	1,453	1,215	939	62		
	$\geq 1 \text{ of } 6$	3,474	546	460	228	3		
Placebo	Both 4	2,531	1,298	1,187	968	41		
	$\geq 1 \text{ of } 5$	3,343	1,464	1,211	939	64		
	$\geq 1 \text{ of } 6$	3,478	536	465	242	7		

eFigure 8. Cumulative incidence of severe rotavirus gastroenteritis by length of interval between doses (both intervals 4 weeks vs. \geq 1 interval of 5 weeks vs. \geq 1 interval of 6 weeks) in the placebo and RV5 vaccinated arms. Number at risk at 12 weeks, 6 months, 12 months, 18 months, and 24 months of age for each arm is below the x-axis.



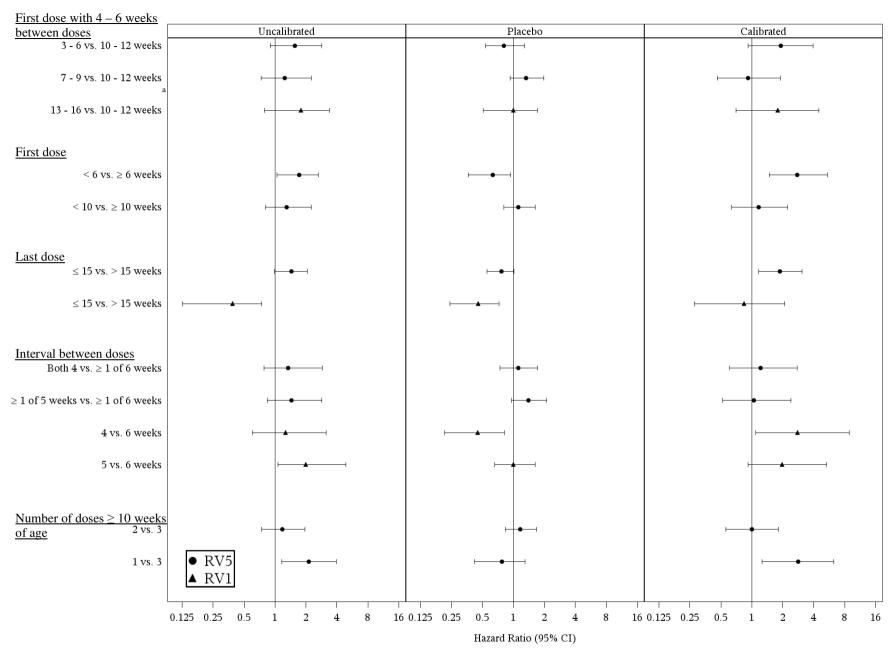
Vaccine Type	Interval between doses (weeks)	N				
RV1	4	1,559	337	169	112	0
	5	1,559	926	631	484	8
	6	1,559	167	93	64	0
Placebo	4	1,553	313	154	96	0
	5	1,553	862	578	455	7
	6	1,553	190	102	67	0

eFigure 9. Cumulative incidence of severe rotavirus gastroenteritis by length of interval between doses (4 weeks vs. 5 weeks vs. 6 weeks) in the placebo and RV1 vaccinated arms. Number at risk at 12 weeks, 6 months, 12 months, 18 months, and 24 months of age for each arm is below the x-axis.

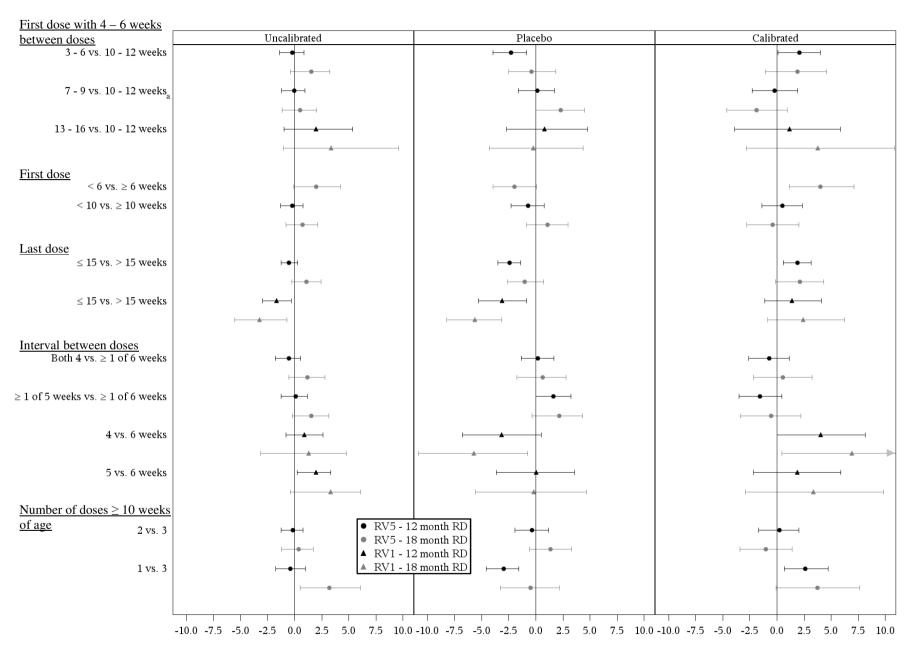


	Number of							
Vaccine	doses ≥ 10	N						
Type	weeks of	N						
	age							
RV5	Zero	1,030	2	0	0	0		
	One	3,666	397	351	200	2		
	Two	3,271	2,432	2,152	1,559	63		
	Three	784	765	640	556	46		
Placebo	Zero	1,029	6	2	0	0		
	One	3,675	405	340	208	0		
	Two	3,279	2,434	2,140	1,532	74		
	Three	780	751	621	535	40		

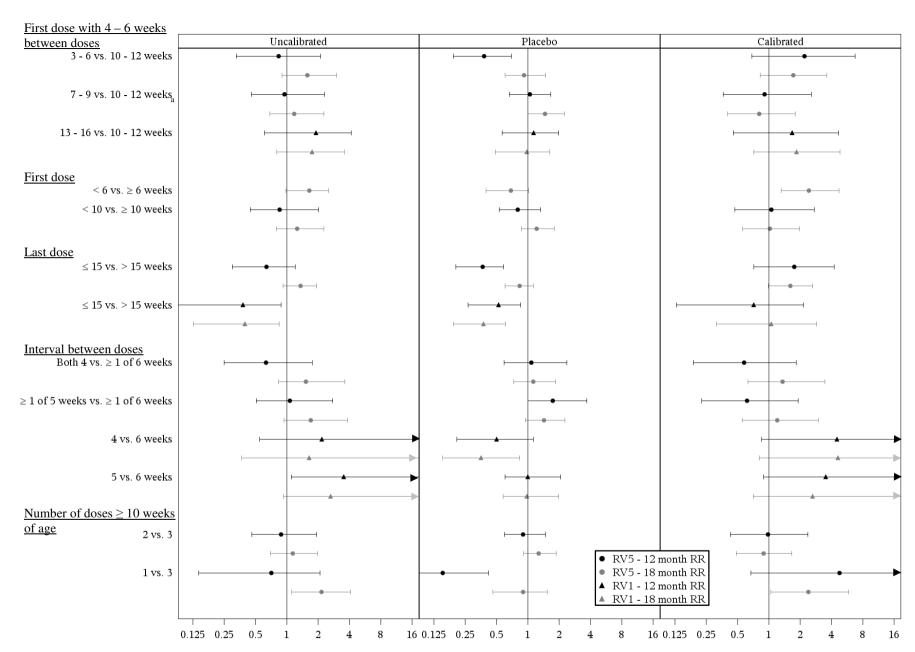
eFigure 10. Cumulative incidence of severe rotavirus gastroenteritis by number of doses received \geq 10 weeks age (zero vs. one vs. two vs. three) in the placebo and RV5 vaccinated arms. Number at risk at 12 weeks, 6 months, 12 months, 18 months, and 24 months of age for each arm is below the x-axis.



eFigure 11. Uncalibrated, placebo arm, and calibrated hazard ratios.



eFigure 12. Uncalibrated, placebo group, and calibrated risk differences.



eFigure 13. Uncalibrated, placebo group, and calibrated risk ratios.